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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/780,035	02/09/2001	Tariq Ghayer	BBC-084	8433

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
03/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/780,035	GHAYER ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,14,15,17-21,26,28-31,33 and 35-60* is/are pending in the application.

4a) Of the above claim(s) *39-43 and 47-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,14,15,17-21,26,28-31,33,35-38 and 44-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/11/2008 has been entered.

2. Applicant's amendment, filed 12/11/2008 has been entered.

Claims 5-10, 12, 16, 22-25, 27, 32, 34 and 61 have been canceled.
Claims 1-4 and 13 have been canceled previously.

Claims 11, 17-21, 26, 28-29, 33, 35, 36 and 44 have been amended.

Claims 11, 14-15, 17-21, 26, 28-31, 33 and 35-60 are pending.

Claims 11, 14-15, 17-21, 26, 28-31, 33, 35-38 and 44-46 are under consideration in the instant application.

Claims 39-43, and 47-60 have been withdrawn as being drawn to the non-elected invention.

3. The amendment filed on 12/11/2008 is considered non-compliant because it fails to meet the requirements of 37 CFR § 1.121, as amended on June 30, 2003 (see 68 Fed. Reg. 38611, Jun. 30, 2003).

The amendment is non-compliant because the "Listing of Claims" is not a complete listing of all of the claims.
The Listing of Claims, filed 12/11/2008 does not include withdrawn claims 39-43 and 47-60.

In order to advance prosecution, this Office Action is set forth,
However, applicant is required to comply with meet the requirements of 37 CFR § 1.121.

4. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

This Office Action will be in response to applicant's amendments/arguments, filed 12/11/2008.

The rejections of record can be found in the previous Office Actions.

Applicant's arguments and the examiner's rebuttal are essentially the same of record.

See the previous Office Actions for a more detailed analysis of applicant's arguments.

5. Upon reconsideration of applicant's amended claims, filed 12/11/2008; the previous rejection under 35 USC 112, second paragraph, with respect to the recitation of "KG1" has been withdrawn.

6. Upon reconsideration of applicant's amended claims and evidence concerning the availability of the KG1 cell line from the ATTC, filed 12/11/2008;
the previous rejection under 35 USC 112, first paragraph, with respect to the recitation of "KG1" has been withdrawn.

7. Upon reconsideration of applicant's arguments and amended claims, filed 12/11/2008;
the previous rejection under 35 USC 112, first paragraph, enablement with respect to the recitation of "at least one amino acid residue" has been withdrawn.

Given applicant's amended claims and arguments, it appears that the claims are not drawn to modifying "at least one amino acid residue" across the entire antibody or antibody regions, but are limited *only at the specific amino acid residues recited in the instant claims*.

8. Claims 26, 28-31, 33, 35- and 44-46 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.
The specification as originally filed does not provide support for the invention as now claimed: "at least one amino acid substitution at a position selected from the group … ".

Applicant's amendment, filed 12/11/2008, does not provide clear guidance to the newly amended claims.

Rather, it appears that applicant relies upon the amino acid substitutions introduced into the specific 2E1 and Lt28 antibodies (e.g., see Tables 7-11 on pages 30-33 of the instant specification).

However, the recitation of "at least one amino acid substitution at a position selected from the recited amino acid positions" is broader than the instant disclosure of providing for certain substituted residues at each of the specific amino acid positions as the claims currently read generically on any amino acid substitution (compare to Tables 7-11 on pages 30-33 of the instant specification).

The instant claims now recite limitations which were not clearly disclosed in the priority applications as well as the specification as-filed, and would have changed the scope of the priority applications and do change the scope of the instant disclosure as-filed.

It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

The specification as filed does not provide a sufficient written description of "at least one amino acid substitution at a position selected from the group … ". The specification does not provide sufficient blazemarks nor direction for the instant methods encompassing the above-mentioned "limitation" as currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action.

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above.
See MPEP 714.02 and 2163.06

9. Claims 11, 14-15, 17-21 and 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kucherlapati et al. (US Patent No. 6,075,181, of record) and Dinarello et al. (J. Leukoc. Biol. 1998, 63:658-664. IDS #A4), for the reasons of record set forth in the previous Office Actions.

Applicant's arguments, in conjunction with basic legal principles of obviousness, filed 12/11/2008, have been fully considered, but are not deemed persuasive for reasons or record set forth in the previous Office Actions and reiterated herein, in part, for applicant's convenience.

Applicant argues the following.

Applicants submit that the above-cited references, either singularly or in combination, do not teach, suggest, or motivate one skilled in the art, to make Applicants' human anti-IL-18 antibodies or methods of making the same as recited by the claims as amended. Dinarello et al. and Kucherlapati et al., either alone or in combination, do not teach or suggest fully human antibodies to human IL-18, nor do Dinarello et al. and Kucherlapati et al. set forth which such antibodies might be bound to or the dissociation constants and activit3f of the antibodies generated. In particular, as required by claim 11 and claims dependent therefrom, Dinarello et al. and Kucherlapati et al. do not teach or suggest an isolated human antibody, or an antigen-binding portion thereof, that binds an epitope of human IL-18, or portion thereof, the epitope comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 33, wherein the antibody, or antigen-binding portion thereof, dissociates from the epitope of human IL-18 with a off rate constant of 0.1 s⁻ or less, as determined by surface plasmon resonance, or inhibits human IL- 18 activity of IFN-~, induction in KG-1 cells (ATCC Accession No. ATCC-CCL-246) with an IC50 of 1 x 106M or less.

In addition, Dinarello et al. and Kucherlapati et al., either alone or in combination, do not teach a human anti-IL-18 antibody that dissociates from human IL-18 with a off rate constant of 0.1 s or less, 1 x 10-2sqor less, 1 x 10-Ss-lor less, 1 x 10-4slor less, 1 x 10Ss-lor less, or 1 x 106slor less as determined by surface plasmon resonance, as required by pending claims 17-21 and 44-46. Further, Dinarello et al. and Kucherlapati et al., either alone or in combination, do not teach an anti-IL-18 antibody that inhibits human IL-18 activity of IFN, induction in KG-1 cells with an ICs0 of 1 x 106M or less, 1 x 107M or less, 1 x 108M or less, 1 x 10-9M or less, 1 x 10l°M or less, or 1 x 10-11M or less, as required by claims 17-21 and 44-46. Still further, Dinarello et al and Kucherlapati et al., either alone or in combination, do not teach a human IL-18 antibody that binds an epitope of human IL-18 comprising an amino acid sequence of either SEQ ID NO: 3 or 33 as required by claims 11, 14, 15, 17-21, and 44-46.

Applicant's arguments and the examiner's rebuttal are essentially the same of record. See the previous Office Actions for a more detailed analysis of applicant's arguments.

Again, applicant's arguments have not been found persuasive for the following reasons.

Again, in response to applicant's continual argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case as noted previously, the teaching, suggestion, or motivation to make the claimed antibody can be readily found in the cited references as Dinarello teaches availability of human IL-18, the involvement of IL-18 in clinical pathology as that antibodies to IL-18 can inhibit the in vivo production of other pro-inflammatory cytokines, and that neutralizing anti-IL-l8 antibodies are a therapeutic option for specific blockade of IL-18.

Additionally as noted previously, Kucherlapati teaches a method of producing fully human monoclonal antibodies to any protein of interest, but especially cytokines, and advantages of such antibodies in avoiding the undesired immune responses elicited by administering non-human antibodies to humans. Therefore, it is instantly obvious to a person having ordinary skill in the art to combine the teachings of the cited references and to make the human anti-IL-18 antibodies as claimed for the purpose of disease treatment using the method taught by Kucherlapati.

Applicant's arguments focusing on dissociation constants and certain functional characteristics of the claims anti-IL-18 antibodies to distinguish the prior art from the instant claims is acknowledged.

However, these characteristics were clearly consistent with deriving neutralizing anti-IL-18 antibodies, including those anti-IL-18 antibodies that could inhibit the in vivo production of other pro-inflammatory cytokines, as a therapeutic option for specific blockade of IL-18 at the time the invention was made.

For example as noted previously, Dinarello clearly teaches (1) the pathological role of IL-18 in disease development as that IL-18 is evolving as a major as a pro-inflammatory cytokine with implications for a role in inflammatory and infectious diseases, and it may also be a player in autoimmune diseases (page 658, the right column), and anti-IL-18 antibodies suitable for treating human diseases, and (2) neutralizing anti-IL-l8 antibodies are a therapeutic option for specific blockade of IL-18.

It has been acknowledged that while Dinarello does not teach a human anti-IL-18 antibody or a method of making such per se, Kucherlapati teaches a method of producing fully human monoclonal antibodies to any protein of interest, but especially cytokines, and advantages of such antibodies.

Again, in contrast to applicant's assertions, the combined teachings provide strong teaching, suggestion, or motivation to arrive at applicant's invention.

Again, applicant has argued that the combination of the cited art is made by the examiner, upon guidance, direction, and motivation to do so, by applicant's present invention, and that this is hindsight reconstruction and is impermissible as a basis for 103 rejection.

Again, this argument has not been found persuasive for the reasons addressed above. In addition, in response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Also, the arguments of counsel cannot take the place of objective evidence in the record. In re Schulze, 145 USPQ 716, 718 (CCPA 1965). See MPEP 716.01(c).

One cannot show nonobviousness by attacking references individually where the rejections art based on combinations of references. In re Keller , 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc. , 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).
See MPEP 2145.

"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdigital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Given that the prior art goal was to provide inhibitory anti-IL-18 antibodies for diagnostic and therapeutic utilities in humans,
incorporating the claimed functional and structural characteristics such as human antibodies with certain dissociation constants and epitopic specificities were implicit as well as routine to the ordinary artisan at the time the invention was made and therefore obvious in designing such inhibitory anti-IL-18 antibodies for human therapeutic / diagnostic utilities

Applicant's arguments have not been found persuasive.

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 11, 14-15, 17-21, 26, 28-31, 33, 35-38 and 44-46 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19-33, 61-63, 75-76, 80-113 of USSN 10/988,360.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The instant and copending claims are drawn to antibodies that bind human IL-18. The copending claims appear to anticipate or render obvious at least the more generic claims of the instant claims (e.g., see instant claims 11, 15, 17-21).

Applicant is invited to clarify the differences from the instant (e.g., see instant claims 26, 28-31, 33, 35-38, and copending claims that recite specific sequences, that is, whether the anti-IL-18 antibodies are obvious variants over one another or not.

Instant claims 44-46 read on anti-IL-18 antibodies that recite specific sequences (see instant claims 26, 28-31, 33, 35-38) and those that do not recite specific sequences (see instant claims 11, 15, 17-21).

12. Claims 11, 14-15, 17-21, 26, 28-31, 33, 35-38 and 44-46 are directed to an invention not patentably distinct from claims 19-33, 61-63, 75-76, 80-113 of USSN 10/988,360 for the reasons above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No., discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phillip Gambel/
Primary Examiner
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Art Unit 1644
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